IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Genoveffa Franchini et al.	Examiner: Jeffrey S. Parkin
Serial No.:	10/048072	Group Art Unit: 1648
Filed:	January 25, 2002	Docket No.: 1662.018US1
Title:	Immunotherapy in HIV Infected Persons Using Vaccines after Multi-Drug Treatment	

DECLARATION UNDER 37 C.F.R. § 1.132

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I, Genoveffa Franchini, declare and say as follows:

1. I am a named co-inventor of the present application and make this Declaration in support of the patentability of the claims of the above-identified application. I received my M.D. from University of Medicine, in Modena, Italy, in 1977 and became a board-certified hematologist in 1981. I am an elected member of the American Society for Clinical Investigation and I am on the editorial/advisory board of AIDS Research and Human Retroviruses, AIDS Reviews, Journal of Virology, and Virology and AIDS Abstracts. I have over 25 years of experience as a scientific researcher in the field of virology, and particularly in the field of Human Immunodeficiency Virus (HIV) vaccine development.

2. In the Office Action mailed December 16, 2004, the Examiner rejected claims 1-10 and 12-17 under 35 U.S.C. § 112 because the Examiner asserted that the invention lacks enablement. According to the Examiner, further data is needed to enable the inventive method in a human.

3. Independent claim 1 is directed to a method of stimulating an HIV1-specific $CD8^+$ response in a human infected with an HIV retrovirus said method comprising:

administering to the human, a recombinant viral vaccine, which enters the cells of the human and intracellularly produces HIV specific peptides for presentation on the cell's MHC class I molecules,

where said peptides are presented in an amount sufficient to stimulate a protective $CD8^+$ HIV structural antigen response, and

where said human

i. has a viral load of less than 10,000 viral copies per ml of plasma and a $CD4^+$ cell count of above 500 cells/ml, and

ii. has been treated with one or more anti-viral agents, which contributed to a lower viral copy and higher $CD4^+$ cell count than before treatment;

where said HIV specific peptides comprise HIV gag, gp120, nef or pol peptides.

Claims 2-10 and 12-17 depend ultimately from, or refer to, the method of claim 1.

4. One of my co-inventors, Dr. James Tartaglia, works at Aventis Pasteur.

5. Aventis Pasteur has been conducting clinical trials that involve immunization of humans with various anti-HIV compositions.

6. One of the clinical trials conducted by Aventis Pasteur is the ACTG5024 clinical trial. A series of slides describing this clinical trial, and results obtained recently, are attached as an Appendix to this Declaration. See "ACTG5054: A Phase II Randomized, Partially-Blinded Trial of ART, HIV-specific Immunizations, and IL-2 Cycles to Promote Efficient Control of Viral Replication" (the "ACTG5054 Trial," Appendix).

7. As described at pages 2-4 of the ACTG5054 Trial provided in the Appendix, human subjects infected with HIV that had been receiving anti-retroviral therapy (ART) were used in the study. Subjects selected for the study had a viral load (VL) of less than 50 and a CD4 count of greater than 350. These patients fall within the description of claim 1 in the present application. The selected subjects were subjected to Analytical Therapy Interruption (ATI) in which they were randomly assigned to one of four groups and then subjected to different treatment regimens. The first group (A) received the pox virus ALVAC (placebo) that encoded no HIV peptides. The second group (B) received a recombinant ALVAC pox virus that encoded

HIV gag, protease, and envelop peptides. The third group (C) received interleukin-2 and the pox virus ALVAC (placebo) that encoded no HIV peptides. The fourth group (D) received interleukin-2 and the recombinant ALVAC pox virus that encoded HIV gag, protease, and envelop peptides. The treatment regimens were administered over 48 weeks, at the times indicated on the time line shown on page 4 (w = week).

8. The results of this clinical trial on human subjects are summarized on pages 5-6 of the ACTG5054 Trial (Appendix). As described on page 5, viral load (VL) was lower during the treatment period in subjects vaccinated with pox virus ALVAC vCP1452 (that encodes the HIV gag, protease and envelope peptides), than in patients that received placebo.

9. In a second trial by Aventis Pasteur, called the Quest Study, the effects of therapeutic immunization of recombinant pox virus vaccines on HIV-1 specific CD4 and CD8 T cell responses was observed. A series of slides describing this clinical trial and results obtained, are attached in the Appendix to this Declaration.

10. Human subjects infected with HIV that had been receiving anti-retroviral therapy (ART) were used in the study. See Appendix, pages 8-9 (Quest Trial). Subjects used for the Quest were not subjected to Analytical Therapy Interruption (ATI) and continued to receive ART. Subjects were randomly assigned to one of three groups and subjected to different treatment regimens. The first group (A) received ART alone and no further treatment. The second group (B) received a recombinant canary pox virus (vCP1452) that encoded HIV gag, protease, and envelop peptides. The third group (C) received recombinant canary pox virus (vCP1452) that encoded HIV gag, protease, and envelop peptides, as well as inactivated HIV viral particles.

11. The results of this Quest clinical trial are summarized on pages 11-12 of the Appendix. As stated on page 11, at 24 weeks post-randomization (W24PR), both CD4 and CD8 cell responses were higher in the patients that received the vCP1452 recombinant canary pox virus that encoded HIV gag, protease, and envelop peptides (Groups B and C), than in patients that did not receive this recombinant poxvirus (Group A). However, there was no statistically significant

difference in HIV-specific CD4 or CD8 T cell numbers by 24 weeks after ART was stopped (W24PS). Furthermore, addition of the inactivated HIV viral particles to the treatment regimen did not have a statistically significant effect upon patient response.

12. Thus, beneficial effects on viral load and/or CD8 responses were observed in patients receiving recombinant poxviruses that express HIV peptides during the ACTG5054 Trial and the Quest Trial.

13. I conclude that one of skill in the art can make and use the compositions and methods described and claimed in U.S. Ser. No. 10/048072 to stimulate a CD+8 response against HIV and reduce HIV viral load.

14. I further declare that all statements made herein of my own knowledge are true, and that all statements made on the information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: May 16, 2005

By: _____
Genoveffa Franchini